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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/722,045	10/04/1996	VIRGINIA FREEMAN	P26,487-A USA	3646

7590 02/27/2007

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EXAMINER	
EBRAHIM, NABILA G	
ART UNIT	**PAPER NUMBER**
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	08/722,045	FREEMAN ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/22/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,13,23 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,13,23 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/22/2006 has been entered.

STATUS OF CLAIMS:

Claims 1, 6, 13, 23, and 25-30 are pending in the application.

STATUS OF THE OFFICE-ACTION: Final

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1, 6, 13, 23, 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparks et al. US 5354556 (Sparks) in view of Paradissis et al. US US 5445829 (Paradissis).

Sparks teaches a controlled release formulation comprising microparticles wherein the particle size average diameter is 0.1 microns or greater (100 nanometer), (see abstract). The controlled release powder includes the same drugs nifedipine (col. 4, line 60), morphine (col. 5, line 3), and biodegradable polylactides (col. 4, line 4). The composition is provided as effervescent tablets (col. 7, line 52). Sparks comprised various drug groups in his invention. For example, he included diltiazem, nefidipine (claim 3), verapamil (col. 4, line 59), morphine, codeine sulfate, dihydrocodeine trartarate, oxycodone, buprenorphine (col. 5, lines 1-5), and captopril (col. 4, line 64).

Though Sparks discloses the microparticles, he did not disclose a microcapsule, however, the specification of the current application defines the term microcapsule as being used to include the terms "microsphere", "microparticles", nanosphere" and "nanoparticle", and adds that these terms do not necessarily refer to any structural relationship between the drug and the encapsulating polymer in a matrix (structure). Rather, these terms simply refer to a particle (micron sized or less) in which the drug is entrapped in a polymer (Specification, page 3, lines 3-9).

In addition, the reference does not disclose the D50 percentage of the 100 and 900 nanometers or the adjusted pH. Using microparticles within the range of D 50 recited by the claims of the instant application with a reasonable expectation of success would have been obvious to one of ordinary skill in the art to advance the uniformity in dissolution and absorption rates since particles of the same or similar size and configuration are known to provide the best release and absorption profiles. In addition, Sparks stated that the particle size might be controlled in a number of ways. For

example, the particles size may be controlled by the rate of mixing, the viscosity during manufacturing, the active ingredient particle size or volatility of the solvent (col. 7, lines 20-25). Since the composition is a controlled-release, it is expected that a skilled artisan would be able to adjust the pH of the formulation. Sparks also disclosed that the micro-particles having an average size of from 0.1 to 125 .mu.m, this particle size encompasses the range disclosed in claim 30 of 200-400 nm.

Sparks did not disclose literally the impact of particle size in controlling drug release.

Paradissis teaches a controlled release drug particle comprising the immediate release particle coated with a dissolution modifying system, examples of the drugs used are narcotics, such as morphine, and codeine and their derivatives; such as oxycodone and hydromorphon; cardiovascular preparations such as diltiazem, propranolol, and nifedepine (col. 4, lines 26+). Paradissis teaches also that it should be noted that the particle size of the particles which are used in finally preparing the invention particles can have a significant impact on the release rate of the drug. First, they assist in making hard granules which improves the binding characteristics of the matrix. Secondly, the particle size affects the final product particle size which can greatly influence the rate at which the polymer hydration or gel formation occurs in the capsule, tablet or particle surface. In general, particle sizes outside the ranges disclosed herein are unsuitable for preparing a controlled release pharmaceutical formulation (col. 7, lines 27+).

Because sparks' teachings included particles in the same size (100 nanometer), the same drugs (diltiazem, nefidipine, verapamil, morphine, codeine sulphate,

dihydrocodeine trartarate, oxycodone, buprenorphine, and captopril) and the same polymer (the polylactide), and Paradissis confirms the importance of the particle size in the drug release it would have been obvious to one of ordinary skill in the art to expand the teaching of Paradissis and adjust the size of the particle range disclosed by Sparks to advance the homogeneity of the composition, its dissolution, absorption rates and release rate since particles of the same or similar size and configuration are known to provide the best dissolution and release- profile. In addition the artisan will be motivated by the disclosure of Sparks that particles size might be controlled in a number of ways like controlling the rate of mixing, the viscosity during manufacturing, the active ingredient particle size or volatility of the solvent (col. 7, lines 20-25).

Declaration Under 37 CFR§ 1.132

3. The Declaration under 37 CFR 1.132 filed 12/22/2006 is insufficient to overcome the rejection of claims 1, 6, 13, 23, 25-30 based upon CFR§103 as set forth in the last Office action because: As shown, the table disclosed in the declaration compares particle size 200-400 Micrometers (according to the present invention) to the particles size of the prior art. It is noted that claim 1 recites a size of 100-900 nm which is less that one micron while claim 30 recites particles size of 200-400nm. Nowhere in the claims there is particle size of 200-400 micrometers.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Response to Arguments

4. Applicant's arguments filed 12/22/06 have been fully considered but they are not persuasive. Applicant argues that:

The present claims require the use of microparticles in the range of 100-900 nm or 200 nm to 400 nm (claim 30) which is a much narrower range that the range of the Sparks patent.

As noted in the non-final office-action, Sparks discloses particle size of 0.1 microns or greater (100 nm). The range is 100nm-225 microns, the range encompasses the range disclosed by the Applicant.

Applicant contends that:

The microparticles of Example 1 of Sparks have a particle size range of 10 micron to 180 micron or 10,000nm to 180,000nm. This does not suggest the making of a microparticle based effervescent composition having a range of sizes of 100-900nm.

To respond: The reference is not limited to the example, it is noted that the claimed invention as a whole must be considered. In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.

Applicant also argues that: There are no examples of an actual effervescent composition in Sparks. The only mention of an effervescent composition is an effervescent tablet, which contains no information as to how the effervescent tablet should be formulated. Claims 1 and 23 both point out that the claimed formulation is

adapted to disperse in water to form an effervescent drink. There is no mention in Sparks of forming an effervescent drink. In col. 7, line 56-59, the resistance of the microparticles to chewing action is noted which suggests that all of the tablets are to be placed in the mouth. This observation is confirmed by the text of Sparks at col. 8, lines 29-32 where Sparks notes that the microparticulate nature of the Sparks formulation provides a good mouth feel for chewable and effervescent tablets due to the absence of a granular sensation.

It has been already noted that the reference is not limited to the examples. In addition, Sparks disclosed effervescent tablets (col. 7, line 52); it is known in the art that this dosage form is added to water to form a drink. The chewing action disclosed Sparks is related to the chewing tablets disclosed in the reference. Effervescent tablets are known in the art to be turned into a drink and not to prepared for chewing (col. 7, lines 52, and 53).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim 2/15/06

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER